

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Inventor: Avner Gal *et al*
Assignee: Integrity Applications Ltd.
Title: A METHOD OF MONITORING GLUCOSE LEVEL
Filed: Concurrently herewith
Attorneys' Docket: 605/1

INFORMATION DISCLOSURE STATEMENT

SIR:

Pursuant to provisions of 37 C.F.R. 1.97 and 1.98, Applicant hereby identifies the U.S. Patents and Publications of which it has knowledge. Applicant makes no representation as to whether or not it has conducted a search and is identifying and disclosing these patents and publications in order to comply with its duty to disclose, pursuant to 37 C.F.R. 1.56. Copies of these patents and publications are enclosed, along with PTO form 1449.

Further, the filing of this Information Disclosure Statement does not constitute an admission that the patents are prior art, or are material to patentability of the subject matter of this invention.

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| <u>Inventor</u> | <u>Pat. No.</u> | <u>Date</u> |
|-----------------|-----------------|--------------|
| Thomas | 5,119,819 | Jun 9, 1992 |
| Gozani | 5,771,891 | Jun 30, 1998 |
| Cho | 5,795,305 | Aug 18, 1998 |
| Cho | 5,924,996 | Jul 20, 1999 |
| Chou | 5,941,821 | Aug 24, 1999 |
| Chou | 6,049,728 | Apr 11, 2000 |
| Matsumura | 5,050,612 | Sep 24, 1991 |
| Rosencwaig | 5,657,754 | Aug 19, 1997 |
| Buchert | 5,666,956 | Sep 16, 1997 |
| Gozani | 5,752,512 | May 19, 1998 |
| Fuller | 5,792,668 | Aug 11, 1998 |
| Pinsky | 6,150,812 | Nov 21, 2000 |
| Eppstein | 6,226,541 | May 1, 2001 |
| Oraevsky | 6,309,352 | Oct 30, 2001 |
| Bauer | 6,322,963 | Nov 27, 2001 |
| Bauer | 6,342,347 | Jan 29, 2002 |
| Chaiken | 6,377,828 | Apr 23, 2002 |
| Oraevsky | 6,405,069 | Jun 11, 2002 |

Thomas teaches a method of monitoring blood glucose, but it is based on only an acoustic velocity measurement based on the two-way travel time of an ultrasound pulse. This is actually an invasive process, as the sensor enters the body through the ear lobe.

Gozani ('891) discloses a non-invasive method for blood analyte measurement. First, there is electrical stimulation of an endogenous tissue and then the detection of the resulting electrical response to the stimulus. One embodiment shows electrical stimulation of a hypoxic peripheral nerve, and then the detection of the resulting Compound Action Potential elsewhere along the nerve.

Cho ('305 and '996) uses combined temperature and measurements of either infrared radiation or thermal conductivity to determine the glucose concentration.

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Chou ('821 and '728) determines the blood glucose by a photoacoustic measurement in which the acoustic pulse is generated by heating the patient's skin with electromagnetic radiation.

Matsumura is directed towards a temperature sensor.

Rosencwaig is directed towards an apparatus that includes "means for selectively inducing a periodic heating at a predetermined frequency ... in a manner to create thermal waves".

Buchert measures glucose level by detecting the infrared radiation naturally emitted by a human body.

Gozani ('512) is a blood analyte concentration monitor, which applies a stimulus to an endogenous tissue.

Fuller determines the concentration of a target chemical by subjecting the specimen to radio frequency electromagnetic components. It teaches in-vivo noninvasive assays of NaCl and glucose in blood based on electromagnetic impedance measurements.

Pinsky detects chemical reactions by utilizing a magnetometer probe to detect a change in the electromagnetic field strength. This is an invasive measurement of blood glucose

Eppstein is directed towards a calibration device for a diagnostic medical instrument whose measurements are based on transmitting electromagnetic or acoustic waves and receiving the reflected waves.

Oraevsky ('352) monitors tissue properties in real time during treatment by using an optoacoustic imaging system.

Bauer ('963 and '347) discloses invasive measurements of blood glucose. This is done in the '963 patent by measurement of changes in induced electromotive force, current or other electrical properties during analyte exposure to the sensor. In the '347 patent the sensor makes use of changes in electrostatic fields associated with macromolecular binding agents during their interaction with analytes.

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Chaiken measures an analyte in a tissue of a subject. It involves contacting the tissue with electromagnetic radiation.

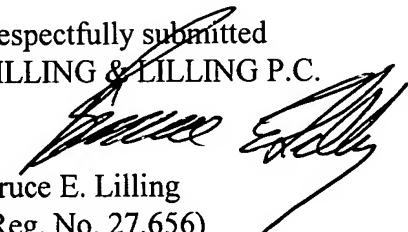
Oraevsky ('069) measures glucose by determining laser-induced profiles of absorbed optical energy distribution in issues via measurements of spatial profile of optically-induced acoustic (pressure) transients using an optoacoustic transducer

Applicant's unique invention is a method of monitoring or measuring the concentration of glucose level in human and animal blood using a non-invasive technique, which includes measurements of the speed of sound through the blood, while inside the body, the conductivity of the blood, by means of electromagnetic inductance, and the heat capacity of the blood, by means of changing the temperature of the measured volume. The instant invention uses measurements of three distinct parameters to determine the blood glucose level, thereby substantially increasing the accuracy of the measurement. None of the prior art techniques disclose any non-invasive method of calculating blood glucose by measuring three separate and distinct blood parameters. Further, none of the prior art methods utilize any measurement of electrical conductivity and heat capacity, which are two of the parameters measured in the instant invention.

Therefore, the instant invention is patentably distinct from, and unobvious in view of, the above patents, whether considered singly or in combination.

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Respectfully submitted
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| INFORMATION DISCLOSURE STATEMENT BY APPLICANT <i>(Use as many sheets as necessary)</i> | | Application Number | |
| | | Filing Date | |
| | | First Named Inventor | Avner GAL |
| | | Art Unit | |
| | | Examiner Name | |
| Sheet 1 of 1 | | Attorney Docket Number | 605/1 |

| U. S. PATENT DOCUMENTS | | | | | |
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